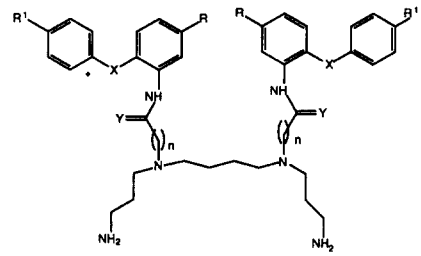
New Spermine and Spermidine Derivatives as Potent Inhibitors of *Trypanosoma cruzi* Trypanothione Reductase

Bioorg. Med. Chem. **1997**, *5*, 1249

Béatrice Bonnet, David Soullez, Elisabeth Davioud-Charvet, Valérie Landry, Dragos Horvath and Christian Sergheraert*
Laboratoire de Chimie des Biomolécules, URA CNRS 1309, Institut Pasteur, Faculté de Pharmacie, 1 rue du Professeur Calmette, 59019 Lille, France

Several spermine and spermidine derivatives containing 2-amino diphenylsulfide substituents were prepared and tested for their inhibiting effects on *T. cruzi* trypanothione reductase. IC_{50} values were assessed between 0.3 and 3 μM. Compound **32** (K_i = 0.4 μM) is the most potent TR inhibitor described so far.



Trioxane Dimers Have Potent Antimalarial, Antiproliferative and Antitumor Activities In Vitro

Bioorg. Med. Chem. **1997**, *5*, 1257

Gary H. Posner,[a,*] Poonsakdi Ploypradith,[a] Whitney Hapangama,[a] Dasong Wang,[a] Jared N. Cumming,[a] Patrick Dolan,[b] Thomas W. Kensler,[b] Donna Klinedinst,[c] Theresa A. Shapiro,[c] Qun Yi Zheng,[d] Christopher K. Murray,[d,*] Lynn G. Pilkington,[d] Lalith R. Jayasinghe,[d] Jeff F. Bray[d] and Randy Daughenbaugh[d]
[a]*Department of Chemistry, School of Arts and Sciences,* [b]*Division of Toxicological Sciences and The Environmental Health Sciences Center, Department of Environmental Health Sciences, School of Hygiene and Public Health, and* [c]*Department of Medicine, School of Medicine, The Johns Hopkins University, Baltimore, MD 21218, U.S.A.* [d]*Synthetic Chemistry Research and Development Group, Hauser Chemical Research Co., Inc., 5555 Airport Boulevard, Boulder, CO 80301, U.S.A.*

A series of tetracyclic and tricyclic trioxane dimers with ether and ester tethers of varying length and flexibility were prepared and found to have potent and potentially therapeutically valuable antimalarial, antiproliferative, and antitumor activities in vitro.

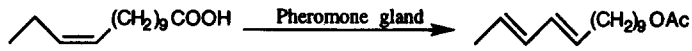
2 Trioxane—OH + X—Linker—X → Trioxane—O—Linker—O—Trioxane

Identification and Biosynthesis of (*E,E*)-10,12-Tetradecadienyl Acetate in *Spodoptera littoralis* Female Sex Pheromone Gland

Bioorg. Med. Chem. **1997**, *5*, 1267

Isabel Navarro, Esther Mas, Gemma Fabriàs* and Francisco Camps
Departament de Química Orgànica Biològica, CID-CSIC, Jordi Girona 18-26, 08034 Barcelona, Spain

A minor component of *Spodoptera littoralis* sex pheromone has been identified as (*E,E*)-10,12-tetradecadienyl acetate. Mass-labeling experiments showed that the (*E,E*)-10,12-tetradecadienoyl moiety is biosynthetically derived from (*Z*)-11-tetradecenoic acid.

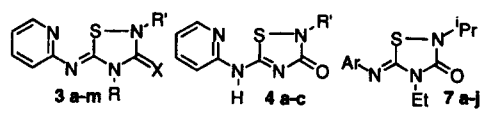


Arylimino-1,2,4-Thiadiazolidinones: A New Family of Potassium Channel Openers

Bioorg. Med. Chem. **1997**, *5*, 1275

Ana Martínez,[a,*] Ana Castro,[a] Ignacio Cardelús,[b] Jesús Llenas[b] and José M. Palacios[b]
[a]*Instituto de Química Médica (CSIC), Juan de la Cierva 3, 28006 Madrid, Spain and* [b]*Laboratorios Almirall S.A., Cardener 68–74, 08024 Barcelona, Spain*

The use of thiadiazolopyridinium chlorides as intermediates in heterocyclic synthesis has led to a new class of potassium channel openers.



Galactosylation with β-Galactosidase from Bovine Testes Employing Modified Acceptor Substrates

Bioorg. Med. Chem. **1997**, *5*, 1285

Ulrike Gambert,[a] Raul Gonzalez Lio,[a,b] Erzsébet Farkas,[a,c] Joachim Thiem,[a] Vicente Verez Bencomo[b] and András Lipták[c]

[a]*Institut für Organische Chemie, Universität Hamburg, Martin-Luther-King-Platz 6, D-20146 Hamburg, Germany*

[b]*Facultad de Quimica, Universidad de la Habana, Cuidad Habana, 10400, Cuba*

[c]*Institute of Biochemistry, Lajos Kossuth University, P.O. Box 55, 4010 Debrecen, Hungary*

Modified acceptor substrates opened further possibilities for the galactosidase-catalyzed synthesis of bioactive disaccharides using β-galactosidase from bovine testes.

Two Non-Racemic Preparations of a Piperidine-Based NMDA Antagonist with Analgesic Activity

Bioorg. Med. Chem. **1997**, *5*, 1293

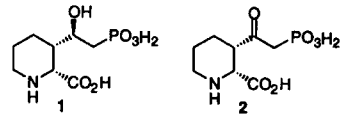
Britt-Marie Swahn,[a] Karin M. Edvinsson,[†] Elisabet Kallin,[a] Ulf Larsson,[b] Odd-Geir Berge,[a] Håkan Molin,[a] Benjamin Pelcman[a] and Alf Claesson[a,*]

[a]*Preclinical Research, Astra Pain Control AB, S-15185 Södertälje, Sweden*

[b]*Chemical Process Development Laboratory, Astra Production Chemicals AB, S-15185 Södertälje, Sweden*

[†]*Present address: Medicinal Chemistry, Astra Hässle AB, S-43183 Mölndal, Sweden*

The non-racemic preparation of **1** is described. The analgesic effects of (±)-**1** and the earlier described (±)-**2** were evaluated using the mouse hot-plate test and the mouse formalin model.

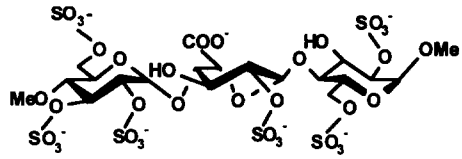


Combined NMR and Molecular Modeling Study of an Iduronic Acid-Containing Trisaccharide Related to Antithrombotic Heparin Fragments

Bioorg. Med. Chem. **1997**, *5*, 1301

Soizic Cros,[a] Maurice Petitou,[b] Philippe Sizun,[c] Serge Pérez[d] and Anne Imberty[d,*]

[a]*Ingénierie Moleculaire, INRA, BP 1627, 44316 Nantes Cédex 03, France;* [b]*SANOFI Recherche, 195 route d'Espagne, 31000 Toulouse, France;* [c]*SANOFI Recherche, 371 rue du Professeur Blayac, 34000 Montpellier, France; and* [d]*CERMAV-CNRS, BP 53, F-38041 Grenoble Cédex 09, France*

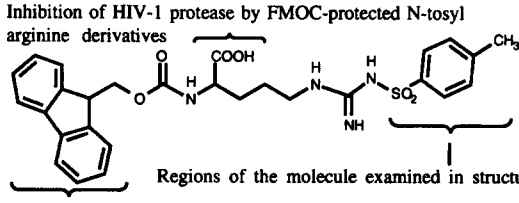


The Discovery, Characterization and Crystallographically Determined Binding Mode of an FMOC-Containing Inhibitor of HIV-1 Protease

Bioorg. Med. Chem. **1997**, *5*, 1311

Earl E. Rutenber,[a] James J. De Voss,[b] Lucas Hoffman,[a] Robert M. Stroud,[a,b] Kwan H. Lee,[b] Juan Alvarez,[b] Fiona McPhee,[b] Charles Craik[a,b] and Paul R. Ortiz de Montellano[b,*]

[a]*Department of Biochemistry and Biophysics and* [b]*Department of Pharmaceutical Chemistry, University of California at San Francisco, San Francisco, CA 94143, U.S.A.*

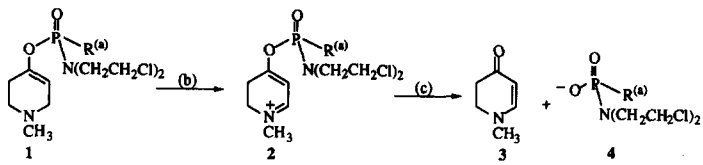


Bioorg. Med. Chem. **1997**, *5*, 1321

Potential Latent Nitrogen Mustard Derivatives Designed to Target Monoamine Oxidase Rich Cells

You-Xiong Wang and Neal Castagnoli, Jr.*
Department of Chemistry, Virginia Tech, Blacksburg, VA 24061-0212, U.S.A.

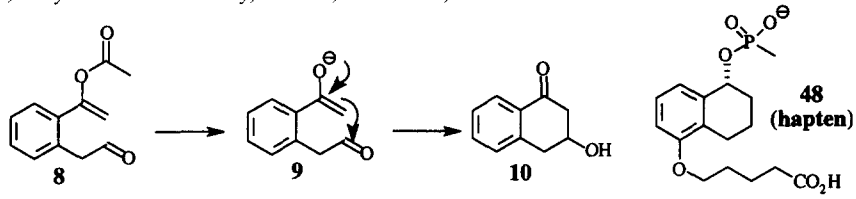
(a) R=NH_2 or $NHCH_2C_6H_5$. (b) Allylic α-carbon oxidation of **1** catalyzed by monoamine oxidase A yields the unstable dihydropyridinium **2**. (c) Spontaneous hydrolysis of **2** forms aminoenone **3** and the cytotoxic phosphoramide mustards **4**.



Bioorg. Med. Chem. **1997**, *5*, 1327

Design and Synthesis of Chiral and Racemic Phosphonate-Based Haptens for the Induction of Aldolase Catalytic Antibodies

YongQi Mu and Richard A. Gibbs*
Department of Pharmaceutical Sciences, Wayne State University, Detroit, MI 48202, U.S.A.

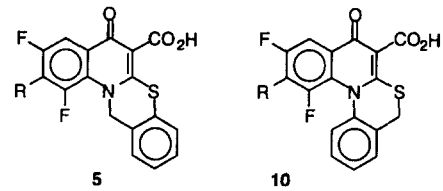


Bioorg. Med. Chem. **1997**, *5*, 1339

Synthesis and Antibacterial Evaluation of [1,3]Benzothiazino[3,2-*a*]quinoline- and [3,1]Benzothiazino[1,2-*a*]-quinoline-6-carboxylic Acid Derivatives

Violetta Cecchetti,[a] Gabriele Cruciani,[b] Enrica Filipponi,[a] Arnaldo Fravolini,[a,]* Oriana Tabarrini[a] and Tao Xin[a]
[a]*Istituto di Chimica e Tecnologia del Farmaco and* [b]*Dipartimento di Chimica, Università di Perugia, 06123 Perugia, Italy*

A series of [1,3]benzothiazino[3,2-*a*]quinoline (**5**) and [3,1]benzothiazino[1,2-*a*]quinoline-6-carboxylic acids (**10**) were synthesized and evaluated for their in vitro antibacterial activity. The activity was discussed in terms of their structural features revealed by molecular orbital correlation.

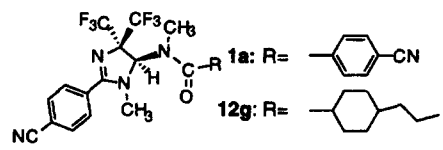


Bioorg. Med. Chem. **1997**, *5*, 1345

Design, Synthesis, and Structure–Activity Relationship Studies of Novel 4,4-Bis(trifluoromethyl)imidazolines as Acyl-CoA: Cholesterol Acyltransferase (ACAT) Inhibitors and Antihypercholesterolemic Agents

Hui-Yin Li,* Indawati DeLucca, George A. Boswell,* Jeffrey T. Billheimer, Spencer Drummond, Peter J. Gillies and Candy Robinson
The DuPont Merck Pharmaceutical Company, Chemical Sciences Division, Experimental Station, Wilmington, DE 19880-0500, U.S.A.

4,4-Bis(trifluoromethyl)imidazolines were discovered as a novel class of stereospecific and potent orally active ACAT inhibitors. This series of imidazolines may be cholesterol and steroidal mimics.

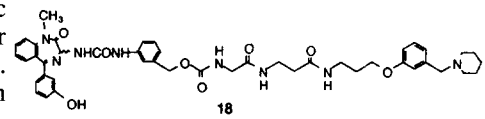


Bioorg. Med. Chem. **1997**, *5*, 1401

Synthesis and Structure–Activity Relationships of Dual Histamine H_2 and Gastrin Receptor Antagonists with Decreased Hydrophobicity

Yasuyuki Kawanishi,* Shoichi Ishihara, Tadahiko Tsushima,* Sanji Hagishita, Michio Ishikawa and Yasunobu Ishihara
Shionogi Research Laboratories, Shionogi & Co., Ltd, Fukushima-ku, Osaka 553, Japan

Two types of hybrid compounds either incorporated with a hydrophilic functionality, e.g. hydroxyl (**18**) or a carboxyl, into the molecule or replaced the C_5 phenyl group with a less hydrophobic functionality, e.g. methyl or hydrogen, were synthesized to decrease their high hydrophobicity and evaluated for the dual activities.



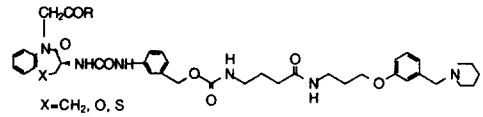
18

Bioorg. Med. Chem. **1997**, *5*, 1411

Synthesis and Structure–Activity Relationships of Dual Histamine H_2 and Gastrin Receptor Antagonists with Modified Benzodiazepine Skeletons

Yasuyuki Kawanishi,* Shoichi Ishihara, Tadahiko Tsushima,* Kaoru Seno, Sanji Hagishita, Michio Ishikawa and Yasunobu Ishihara
Shionogi Research Laboratories, Shionogi & Co., Ltd, Fukushima-ku, Osaka 553, Japan

Dual histamine H_2 and gastrin receptor antagonists with a benzazepine, benzoxazepine, or benzothiazepine moiety as their gastrin receptor antagonist pharmacophores were synthesized and evaluated for the dual activities.

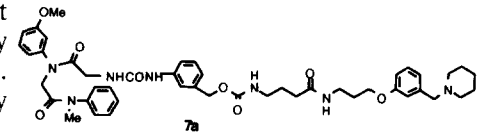


Bioorg. Med. Chem. **1997**, *5*, 1425

Synthesis and Structure–Activity Relationships of Dual Histamine H_2 and Gastrin Receptor Antagonists with Noncyclic Gastrin Receptor Antagonistic Moieties

Yasuyuki Kawanishi,* Shoichi Ishihara, Ryuichi Kiyama, Sanji Hagishita, Tadahiko Tsushima,* Michio Ishikawa and Yasunobu Ishihara
Shionogi Research Laboratories, Shionogi & Co., Ltd, Fukushima-ku, Osaka 553, Japan

A new type of dual histamine H_2 and gastrin receptor antagonist with a noncyclic dipeptide-type gastrin receptor antagonistic moiety was synthesized and the dual antagonistic activities evaluated. Compound **7a** displayed distinct oral gastric acid antisecretory activities with dose–response relationships for the first time.

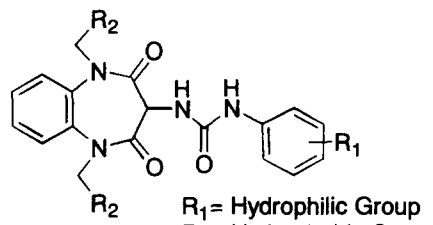


7a

Bioorg. Med. Chem. **1997**, *5*, 1433

Potent and Subtype-Selective CCK-B/gastrin Receptor Antagonists: 2,4-Dioxo-1,5-benzodiazepines with a Plane of Symmetry

Sanji Hagishita,* Kaoru Seno, Susumu Kamata,* Nobuhiro Haga, Yasunobu Ishihara,* Michio Ishikawa and Mayumi Shimamura
Shionogi Research Laboratories, Shionogi & Co., Ltd, Fukushima-ku Osaka, 553, Japan



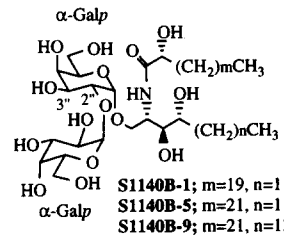
Immunostimulatory Activities of Mono- or Diglycosylated α-Galactosylceramides

Bioorg. Med. Chem. **1997**, *5*, 1447

Akira Uchimura, Toshiyuki Shimizu, Miiko Nakajima, Hitomi Ueno, Kazuhiro Motoki, Hideaki Fukushima, Takenori Natori and Yasuhiko Koezuka*

Pharmaceutical Research Laboratory, Kirin Brewery Co., Ltd, 3 Miyahara-cho, Takasaki-shi, Gunma 370-12, Japan

We examined the effects of 2″- or 3″-monoglycosylated α-GalCers and 2″,3″-diglycosylated α-GalCers on allogeneic MLR and the proliferation of murine spleen cells, and found that their ceramide portions greatly affect their immunostimulatory activities, and that the 3″-hydroxyl group plays a more important role in the immunostimulatory effects of α-GalCer derivatives than the 2″-hydroxyl group.



S1140B-1; m=19, n=11
S1140B-5; m=21, n=11
S1140B-9; m=21, n=13